

Letters to the Editors

Reproducibility of grading systems for breast carcinoma

I wonder if I might be allowed to comment on the paper by Stenkivist *et al.*¹ in the October issue of your journal?

The paper analyses the reproducibility of subjective grading systems for breast carcinoma, using those of WHO^{2,3} and the one I published in 1971. It is obvious that a great deal of work has gone into the paper, both at the microscope and on computer level. However, some points need to be raised concerning the use of the latter typing system. Firstly, Stenkivist *et al.*, describing their use of the system, note that each factor was examined at a magnification of 400. Reference to my paper will show that it was essential that the tumours were 'classified from groups of cells that stood out on low power as cells nearest to the type seen in tumours recurring 10 years or more after operation, irrespective of the findings elsewhere on the slide'. It is to these cells that the criteria apply; that is to say, one must first select a field on low power before the criteria can be studied on high power. When the cells are not in groups they do not express their characteristic morphology (see Table III of Hartveit).⁴

Stenkivist *et al.* also note that 'Hartveit's parameters gave rise to a number of combinations from 3111 (I) to 1333 (III). All intermediate types (79 alternatives) were categorised as type II'. This is a much more rigid application of the criteria than has been described previously when 'an intermediate pattern was accepted as type I or III if it differed by one grade only. For example: $- + \pm 1$ would be accepted as type I ($- + + 1$), $+ - \pm 2$ would be accepted as type III ($+ - - 3$) while $+ \pm + 2$ stays type II whatever'.

Further, I would like to point out that the majority of breast carcinomas I have seen are of type I. Type III is better represented in our necropsy material than type II.⁴ In surgical specimens, type I again predominates, while type III is very rare. Turner and Berry⁵ found: type I 83%, type II 17%, and type III 0%, while Maehle and Hartveit⁶ found: type I 89%, type II 10%, and type III 1%. In the material analysed one would thus expect at most two type III cases, the remainder being mainly type I. The more

rigid use of the criteria mentioned above and, probably (this is not clear from the text), classification on the basis of infiltrating cells rather than cell groups could well explain that all the cases landed in type II.

In conclusion, while it is of interest to note the relationship of nuclear lobulation to the other systems analysed, the system could not be expected to stratify the material used (176 surgical specimens) 'into three categories of tumours'.

F HARTVEIT

The Gade Institute,
Department of Pathology,
University of Bergen,
Norway

References

- Stenkivist B, Westman-Naeser S, Vegelius J, *et al.* Analysis of reproducibility of subjective grading systems for breast carcinoma. *J Clin Pathol* 1979;**32**:979-85.
- Scarff RW, Torloni H. Histological typing of breast tumours. (*International Classification of Tumours, No. 2.*) Geneva: WHO, 1968.
- Black MM, Speer FD. Nuclear structure in cancer tissues. *Surgery, Gyn Obstet* 1957;**105**:97-102.
- Hartveit F. Prognostic typing in breast cancer. *Br Med J* 1971;**4**:253-7.
- Turner DR, Berry CL. A comparison of two methods of prognostic typing in breast cancer. *J Clin Pathol* 1972;**25**:1053-5.
- Maehle BO, Hartveit F. Prognostic typing in breast cancer. *J Clin Pathol* 1973;**26**:784-91.

The authors reply as follows:

Concerning the comment of Dr Hartveit on our paper, we found that all the grading systems we studied had a significant but low reproducibility. Included in this study were the various components of the grading systems we analysed. We also applied the method of Dr Hartveit as she describes it in her letter, although we could not find a higher reproducibility of her grading system when compared with the other grading systems. We think that it is extremely difficult, or even impossible, for any human being to reproducibly remember and strictly adhere to the characterisation of complex nuclear population textures. However, computers are most valuable for such tasks. We have

performed a study of reproducibility of nuclear morphometry using computers¹ and concluded that computerised nuclear morphometry can be a remarkably useful aid in helping the pathologist to more exact grading of the malignancy of a tumour. This was also the opinion of a working group at Dahlem Konferenzen in Berlin last year.² The usefulness of computers in recognising nuclear texture not perceptible by humans is further underlined by studies performed by Julesz *et al.*³

BJÖRN STENKIVIST

Department of Clinical Cytology,
University Hospital,
S-750 14 Uppsala,
Sweden

References

- Stenkivist B, Westman-Naeser S, Holmquist J, *et al.* Computerized nuclear morphometry as an objective method for characterizing human cancer cell populations. *Cancer Res* 1978;**38**:4688-97.
- Stenkivist B, Pressman N, Bartels PH, *et al.* Biomedical pattern recognition and image analysis of cells and tissues. In: Dahlem Konferenzen Series, *Biomedical Image Analysis and Pattern Recognition*, Berlin, 1979.
- Julesz B, Gilbert EN, Shepp LA, Frish HL. Inability of humans to discriminate between visual textures that agree in second-order statistics-revisited. *Perception* 1973;**2**:391-405.

Cyanmethaemoglobin Reference Preparations

The publication of specifications¹ for Cyanmethaemoglobin Reference Preparation by the International Committee for Standardization in Haematology (ICSH), and agreed by the World Health Organization, was a significant advance in quality assurance of haemoglobin measurement. These specifications have been adopted universally as a means of attaining good inter and intra laboratory comparability of haemoglobin. The ICSH protocol specifies that the preparation must be dispensed in sealed 10 ml ampoules of amber glass under sterile conditions. There are valid reasons for this requirement,

Letters to the Editors

namely, the need to ensure that sterility is maintained and evaporation avoided. It follows that material offered in screw-capped bottles is unreliable and does not conform to the specifications. We wish to draw the attention of those working in haematology departments to this matter.

SM LEWIS, *Organiser,*
General Haematology Quality Assurance
 NK SHINTON, *Chairman,*
British Committee for Standards in Haematology

Reference

¹ International Committee for Standardization in Haematology. Recommendations for reference method for haemoglobinometry in human blood (ICSH Standard EP 6/2: 1977) and specifications for international haemoglobincyanide reference preparation (ICSH Standard EP 6/3: 1977). *J Clin Pathol* 1978;31:139-43.

Hydatid disease in mid-Wales

Although there are comparatively few deaths from hydatid disease in Wales, it has been suggested that this small number may be the tip of an iceberg.¹ The disease is not notifiable so it is difficult to obtain accurate figures as few surveys have been undertaken.

Recent local discussion has therefore prompted us to report previously unpublished work on individuals from rural and urban parts of the Principality.

Volunteer blood donors, residents of old people's homes, and local authority employees were involved. All were well, and there was no clinical evidence of hydatid infection. A small blood sample was collected from blood transfusion volunteers at the same time as the blood for transfusion was taken and transported to the laboratory. Sera from individuals (from old people's homes and from county council offices) who had taken part in studies of influenza vaccine^{2,3} were also used.

The complement fixation test⁴ was performed on all specimens. The antigens used comprised hydatid cyst fluids obtained under sterile conditions from cysts in sheep at the Cardiff abattoir. At the laboratory, fluids containing many scolices were centrifuged at 1500 rpm for 10 minutes. Merthiolate 1:10 000 was added to the supernatant fluid which was then stored at +4°C until needed. The antigen was standardised by the usual chessboard technique with individual sera from proven human cases of hydatid disease; 2½ units (MHD) of complement were used. Fixation was allowed to take place at 4°C overnight. The optimal dilution of hydatid fluid was noted, and a dilution suitable for use was thus selected.

The results are shown in Tables 1 and 2. It can be seen that overall only a small number of positive results were obtained and that the titres were low. In only one case was a titre of 1:8 obtained.* Individuals in rural areas, however, had a larger percentage of positive results than those in urban communities. Among the latter there were more positive results from elderly individuals (in old people's homes) than from those in the younger age groups (from Cardiff County Hall).

The results suggest that there is more evidence of contact with *Echinococcus granulosus* in mid-Wales than in urban areas of the Principality. Previous work, however, indicates that this effect is more striking in the farming community⁵ or among those who knew of the disease from personal experience¹ than in the general rural population as sampled here. Further surveys may establish a more precise incidence among the latter.

CHL HOWELLS
Regional Public Health Laboratories
 RJ TAYLOR
Department of Medical Microbiology,
University Hospital of Wales,
Heath Park, Cardiff CF4 4XW

References

- ¹ Clarkson MJ. Hydatid disease in Wales: 2. Eradication. *Vet Rec* 1978;102:259-61.
- ² Howells CHL, Evans AD, Vesselinova-Jenkins CK. Effect of two doses of influenza vaccine in stimulating antibodies in volunteers. *Lancet* 1973;1:1436-8.
- ³ Howells CHL, Vesselinova-Jenkins CK, Evans AD, James J. Influenza vaccination and mortality from bronchopneumonia in the elderly. *Lancet* 1975;1:381-3.
- ⁴ Bradstreet CMP, Taylor CED. Technique of complement fixation test applicable to the diagnosis of virus diseases. *Monthly Bull Minist Health* 1962;21:96-104.
- ⁵ Bradstreet CMP. A study of two immunological tests in the diagnosis and prognosis of hydatid disease. *J Med Microbiol* 1969;2:419-33.

Table 1

Centre	Specimens examined		Percentage
	Total	Positive	
<i>Urban</i>			
Cardiff County Hall	248	2	0.8
Cardiff Old People	125	3	2.4
Pembroke	255	5	1.96
<i>Rural</i>			
Machynlleth	72	4	5.5
Newcastle Emlyn	138	8	5.7
Llanidloes	81	4	4.9
Total	919	26	2.82

Table 2

Titre	Cardiff County Hall	Cardiff old people's homes	Machynlleth	Llanidloes	Newcastle Emlyn	Pembroke
1:2	2	3	4	2	7	4
1:4				1	1	1
1:8				1		
Total	2	3	4	4	8	5

*According to Bradstreet,⁵ a low titre of antibody may occur in human infection if the cyst is deficient in scolices and thus in the antigen contained therein. Low titres may also occur if the cyst is surrounded by fibrous or calcified tissue preventing the escape of antigen into the circulation.